

III. Remarks

A. Status of the Application

Claims 3 and 5-8 are under examination. Claims 1-2 and 9-31 have been withdrawn from consideration. Claims 3 and 5 have been amended. Claim 4 has been cancelled. Favorable consideration and allowance of claims 3 and 5-8 in view of the foregoing amendments and the following remarks are respectfully requested.

B. Information Disclosure Statement Filed July 6, 2004

Attached as Exhibit A is a copy of an Information Disclosure Statement filed July 6, 2004. Attached as Exhibit B is a copy of a postcard receipt which confirms that the Information Disclosure Statement filed July 6, 2004 was received in the mailroom of the United States Patent and Trademark Office on July 8, 2004. It is respectfully requested that the Examiner consider the references cited in the Information Disclosure Statement filed July 6, 2004 and initial and return to the undersigned the modified PTO-1449 Forms attached thereto confirming the Examiner's consideration of such references.

C. Rejections Under 35 U.S.C. §112

Claims 5 and 8 stand rejected under 35 U.S.C. §112, second paragraph for indefiniteness. Insofar as it may be applied against the present claims, this rejection is respectfully traversed.

Claim 5 has been amended to positively recite that the saccharides set forth in claim 3 are predigested.

Claim 8 is rejected because the claim allegedly lacks antecedent basis for the term "biological" digestion. Claim 5, from which claim 8 depends, recites that "the saccharides are predigested by a digestion technique selected from physical digestion, chemical digestion and biological digestion". Claim 8 recites that the biological digestion is conducted with "microbes selected from the group consisting of bacteria, fungi and molds". Contrary to what is alleged in the Office action, there is clear antecedent basis for all of the subject matter of claim 8.

In light of the foregoing amendments and remarks, the rejections of claims 5 and 8 under 35 U.S.C. §112, second paragraph should be withdrawn.

D. Claim Objections

Claim 8 is objected to under 35 U.S.C. §1.75(c) as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. This objection is respectfully traversed.

As noted above, Claim 5 from which claim 8 depends, recites that “the saccharides are predigested by a digestion technique selected from physical digestion, chemical digestion and biological digestion”. Claim 8 recites that the biological digestion is conducted with “microbes selected from the group consisting of bacteria, fungi and molds”. The Office action suggests that claim 8 should be dependent upon claim 4. This is incorrect. Claim 8 is properly dependent upon claim 5. There is clear antecedent basis for the terms of claim 8 in claim 5 and claim 8 further limits the subject matter of claim 5 by specifying the method by which the biological digestion of saccharides is conducted.

For the foregoing reasons, the objection to claim 8 should be withdrawn.

E. Rejections Under 35 U.S.C. §102(b)

Claim 3 stands rejected under 35 U.S.C. §102(b) over PCT International Publication No. WO9506068 to Yamada et al. (“Yamada ‘068”) Insofar as it may be applied against the present claim, this rejection is respectfully traversed.

As provided in MPEP § 2131, “[t]o anticipate a claim, the reference must teach every element of the claim . . .”. Therefore, Yamada ‘068 must disclose all of the elements of claim 3 to sustain this rejection. However, Yamada ‘068 does not meet the standard required by MPEP § 2131 because Yamada ‘068 does not disclose or suggest each and every element of claim 3.

Specifically, independent claim 3 is drawn to a method for producing correctly structured and properly functioning glycoproteins and/or glycolipids in a human that includes administering to a subject a dietary supplement comprising a nutritionally effective amount of at least two saccharides selected from the group consisting of galactose, glucose, mannose, N-acetylneuraminic acid, fucose, N-acetylgalactosamine, N-acetylglucosamine, xylose, arabinose, glucuronic acid, galacturonic acid, iduronic acid, arabinogalactan, acetylated mannose, glucosamine and galactosamine, wherein prior to administration, oligomeric or polymeric forms of the at least two saccharides are predigested into a mixture of monosaccharides and oligosaccharides.

Yamada '068 discloses the administration to humans of a polysaccharide containing arabinose, galactose, glucose, rhamnose, galacturonic acid and glucuronic acid as the constituent sugars thereof to improve hematopoietic function and to serve as a radioprotective agent for treating or preventing radiation injury. Contrary to the method of claim 3, however, Yamada '068, does not disclose, suggest or motivate the predigestion of such polysaccharides into a mixture of monosaccharides and oligosaccharides prior administration thereof to a human. As has been discussed extensively in the prosecution of parent application no. 09/242,215, by predigestion the Applicants mean that the oligomeric or polymeric saccharides are at least partially predigested into the monomeric forms thereof. Examples of ways of achieving such predigestion are taught in the specification of the present application.

The test for anticipation under 35 U.S.C. §102(b) is whether a single reference literally reads on the claim; what the reference broadly teaches is not the issue; any differences between the claimed invention and the reference are sufficient to prevent a 102 rejection. See *Constant v. Advanced Micro-Devices, Inc.*, 7 USPQ2d 1057 (Fed. Cir. 1988). For the foregoing reasons, Yamada '068 does not anticipate the method of claim 3. Accordingly, it is requested that the rejection of claim 3 under 35 U.S.C. §102(b) over Yamada '068 be withdrawn.

Claims 3-6 stand rejected under 35 U.S.C. § 102(b) over European Patent Application No. 561,408 to Uchida ("Uchida '408"). As noted above, claim 4 has been cancelled. Insofar as it may be applied against claims 3 and 5-6, this rejection is respectfully traversed.

As provided in MPEP § 2131, "[t]o anticipate a claim, the reference must teach every element of the claim ...". Therefore, Uchida '408 must disclose all of the elements of claims 3 and 5-6 to sustain this rejection. However, Uchida '408 does not meet the standard required by MPEP § 2131 because Uchida '408 does not disclose or suggest each and every element of claims 3 and 5-6.

Specifically, independent claim 3 is drawn to a method for producing correctly structured and properly functioning glycoproteins and/or glycolipids in a human that includes administering to a subject a dietary supplement comprising a nutritionally effective amount of at least two saccharides selected from the group consisting of galactose, glucose, mannose, N-acetylneuraminic acid, fucose, N-acetylgalactosamine, N-acetylglucosamine, xylose, arabinose,

glucuronic acid, galacturonic acid, iduronic acid, arabinogalactan, acetylated mannose, glucosamine and galactosamine, wherein prior to administration, oligomeric or polymeric forms of the at least two saccharides are predigested into a mixture of monosaccharides and oligosaccharides.

Uchida '408 discloses the administration to humans of a polysaccharide having a β -1,3-glucoside bond in the main chain such as sizofiran, lentinan, pachyman, pachmaran, paramylon, leucosin, xylan, dulxylan, curdlan, succinoglucan, sclerotan, scleroglucan, xanthan gum, laminaran, and pendulan for treating chronic fatigue syndrome. As disclosed in Column 4, lines 7-12 of Uchida '408, it is difficult to purify sizofiran because it is a highly viscous and thixotropic material and that "it is therefore preferable to lower its molecular weight without changing the basic structure of the polysaccharide." Uchida '408 mentions that the molecular weight of sizofiran can be lowered without changing its basic structure by ultrasonic treatment and high-shear treatment of a liquor containing sizofiran.

Contrary to the method of claim 3, however, Uchida '408, does not disclose, suggest or motivate the predigestion of a polysaccharide such as sizofiran into a mixture of monosaccharides and oligosaccharides prior administration thereof to a human. Instead, Uchida '408 discloses the administration of a polysaccharide and that when purifying a highly viscous and thixotropic polysaccharide such as sizofiran it is desirable to reduce the molecular weight thereof by ultrasonic treatment or high-shear treatment without changing the basic structure of the polysaccharide.

The test for anticipation under 35 U.S.C. §102(b) is whether a single reference literally reads on the claim; what the reference broadly teaches is not the issue; any differences between the claimed invention and the reference are sufficient to prevent a 102 rejection. See *Constant v. Advanced Micro-Devices, Inc.*, 7 USPQ2d 1057 (Fed. Cir. 1988). For the foregoing reasons, Uchida '408 does not anticipate the method of claim 3 or the methods of claims 5-6 which depend from and include the subject matter of claim 3. Accordingly, it is requested that the rejection of claims 3 and 5-6 under 35 U.S.C. §102(b) over Uchida '408 be withdrawn.

F. Rejections Under 35 U.S.C. §103(a)

Claim 3 stands rejected under 35 U.S.C. §103(a) over Murray et al. (AQ or V, Robert K. Murray et al., Harper's Biochemistry, Appleton & Lange, 1996, pages 648-649), hereinafter

referred to as “Murray”. Insofar as it may be applied against the present claims, this rejection is respectfully traversed.

To sustain the present rejection of claim 3 under 35 U.S.C. § 103(a), a prima facie case of obviousness must be established. MPEP § 2142 provides that a prima facie case of obviousness requires three basic criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. In the present case, none of the criteria set forth in MPEP § 2142 have been satisfied with respect to claim 3.

Murray discloses the principal sugars found in human glycoproteins, however, Murray does not teach, suggest or motivate a method for producing correctly structured and properly functioning glycoproteins and/or glycolipids in a human by administering a dietary supplement comprising a nutritionally effective amount of at least two saccharides. Instead, Murray discloses the end product, i.e. glycoproteins.

In contrast, the claimed method is directed to the administration of the starting ingredients that ultimately lead to the glycoprotein end products. Prior to the claimed method, the conventional wisdom in the art was subject to the “glucose dogma”, according to which every saccharide can be biochemically synthesized from glucose. Instead, the claimed method eliminates the need to synthesize glucose from biochemical precursors, and only then, synthesize the various saccharides needed for glycoprotein synthesis by providing the saccharides directly in nutritionally effective amounts. The “glucose dogma” assumes that all precursors and enzymes necessary for synthesis of hundreds of different saccharide derivatives, are all available, at all times, in sufficient amounts, at the necessary locations. The present invention reduces the need for all these precursors and enzymes, in a multitude of locations, by providing the missing saccharides “in nutritionally effective amounts,” hence, breaking through the “glucose dogma.”

In addition and contrary to the method of claim 3, Murray does not disclose, suggest or motivate the predigestion of oligomeric or polymeric forms of saccharides into a mixture of monosaccharides and oligosaccharides prior administration thereof to a human.

Consequently, Murray fails to disclose, suggest or motivate all of the elements of claim 3. Accordingly, at least one of the required elements of the prima facie case has not been satisfied, and therefore the prima facie case must fail.

Murray also fails to satisfy the remaining elements of the prima facie case. There is no suggestion or motivation, either in Murray or in the knowledge generally available to one of ordinary skill in the art, to modify Murray to arrive at the subject matter of claim 3. Further, even if such modification was possible, in light of the “glucose dogma” that prevailed at the time the invention was made, there could be no reasonable expectation of success that the result would be the subject matter of claim 3.

In view of the foregoing, Applicants submit that a prima facie case of obviousness over Murray has not and cannot be established with respect to claim 3. Accordingly, Applicants respectfully request that the rejection of claim 3 under 35 USC § 103(a) over Murray be withdrawn.

Claims 3-8 stand rejected under 35 U.S.C. § 103(a) over Murray in view of Beldman et al., “Enzymic Hydrolysis of Beer Brewer’s Spent Grain and the Influence of Pretreatments”, hereinafter referred to as “Beldman”, Remington, “Breakfast, Invalid and Infant Food”, hereinafter referred to as “Remington” and Uchida ‘408. As noted above, claim 4 has been cancelled. Insofar as it may be applied against claims 3 and 5-8, this rejection is respectfully traversed.

To sustain the present rejection of claims 3 and 5-8 under 35 U.S.C. § 103(a), a prima facie case of obviousness must be established. MPEP § 2142 provides that a prima facie case of obviousness requires three basic criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. In the present case, none of the criteria set forth in MPEP § 2142 have been satisfied with respect to claims 3 and 5-8.

The deficiencies of Murray and Uchida ‘408 with respect to the subject matter of claim 3 are set forth above.

Remington merely discloses cooking raw cereals, a process which does not provide for the administration to humans of a dietary supplement that includes nutritionally effective amounts of at least two saccharides, in which prior to such administration the oligomeric or polymeric forms of such at least two saccharides are predigested into a mixture of monosaccharides and oligosaccharides. In fact, even after the “treatment” afforded the fibers in Remington, Remington acknowledges that the “cell walls have not been broken to any great extent in the milling process,” thereby requiring additional cooking. Remington, page 155, Col. 2, line 18-20. In addition, Remington discloses on page 155, column 2, line 23 to page 156, column 1, line 23, that rolled and flaky preparations of cereals contain soluble starch, not soluble saccharides. (see also, Col. 1, examples listed (i) to (vi)).

In contrast, claim 3 is drawn to a method for producing correctly structured and properly functioning glycoproteins and/or glycolipids in a human comprising administering to a subject a dietary supplement comprising “a nutritionally effective amount” of at least two saccharides wherein the at least two saccharides are predigested into a mixture of monosaccharides and oligosaccharides.

Neither Remington alone, nor its combination with Murray and/or Uchida ‘408 provide any teaching of either a “nutritionally effective amount” or of the predigestion of an oligomeric or polymeric form of a saccharide into a mixture of monosaccharides and oligosaccharides.

Beldman merely discloses the enzymatic hydrolysis of spent grain by commercial cellulases. However, Applicants note that Beldman discloses on page 669, Table 3, that the sugar composition of spent grains after 2.0 N sulfuric acid hydrolysis included varying amounts of arabinose, xylose, mannose, galactose and glucose, depending upon subsequent treatment either by drying, extraction with ethanol or extraction with water. While Table 3 includes a line item for rhamnose and fucose, the table discloses that the amount of such sugars in the various compositions is 0%, which are hardly nutritionally effective amounts. Moreover, enzymatic hydrolysis of spent grain by commercial cellulases according to Beldman resulted in a range of polysaccharide hydrolysis from 41-47%.

First and foremost, Beldman does not provide any teaching or enablement of a “nutritionally effective amount” of anything, much less of a dietary supplement that provides at least two saccharides to a subject. There is no teaching of the preparation of any supplement. In

fact, the use of harsh hydrolysis (e.g., 2.0 N sulfuric acid) and treatment with strong bases (4 M KOH) strongly militate against the use of any remaining saccharides for anything other than simple, mere characterization. Nor does enzymatic treatment with cellulases from a pathogen such as trichoderma teach, suggest or motivate the administration to a subject of a nutritionally effective amount of the saccharides claimed herein. Quite to the contrary, Beldman merely characterizes the components without any indication, teaching, suggestion, enablement or motivation that any of the saccharides that may be contained may be administered as a dietary supplement. Furthermore, Beldman does not provide any teaching or enablement for modifying the content of the saccharides to provide “a nutritionally effective amount” thereof or to provide for the predigestion of oligomeric or polymeric forms of the saccharides into a mixture of monosaccharides and oligosaccharides.

Thus, none of Murray, Beldman, Remington or Uchida ‘408 disclose, suggest or motivate the method of claim 3.

To complete the analysis under 35 U.S.C. § 103(a), the third criteria of a prima facie case of obviousness is whether the references teach, suggest or motivate the invention. It is clear, as noted above, that Murray, Beldman, Remington and Uchida ‘408, alone or in combination, fail to disclose or suggest all of the limitations of claim 3. Nor is there any indication, whatsoever, that the references point to each other for teachings that would combine to achieve the present invention. Without a proper suggestion or motivation for modification of Murray to include the subject matter of one or more of Beldman, Remington and Uchida ‘408, there could be no reasonable expectation of success.

Moreover, it is respectfully submitted that the combination of Murray, Beldman, Remington and Uchida ‘408 is improper. According to MPEP § 2143.01, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Since the Federal Circuit first addressed this issue in *ACS Hosp. Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 221 USPQ 929 (Fed. Cir. 1984), the Federal Circuit has consistently held that:

Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so.

ACS Hosp. Systems, Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)); *In re Fritch*, 23 USPQ 2d 1780, 1783-1784 (Fed. Cir. 1992).

Also, the case law is clear that there must be evidence that a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed. It is also clear that a rejection cannot be predicated on the mere identification of individual components of claim limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *Ecolchem Inc. v. Southern California Edison*, 56 USPQ2d 1065, 1076 (Fed. Cir. 2000). Here, no such evidence has been presented. Applicants respectfully request that any such evidence be made of record with precise citations or that the rejections based on all these references be withdrawn. In addition, there is absolutely no teaching, suggestion or motivation to support the combination of Murray, Beldman, Remington and Uchida '408.

The current case law makes it clear that the best defense against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references. See *In re Dembiczak*, 50 USPQ2d, 1614, 1617 (Fed. Cir. 1999). "Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability – the essence of hindsight." *Id.* It is respectfully submitted that the only way Murray, Beldman, Remington and Uchida '408 could be pieced together to defeat patentability is indeed to use Applicant's disclosure as a blueprint. Therefore, the combination of references is improper.

In addition, as the Federal Circuit has recognized, “standards for the patenting of chemical entities have evolved.” *In re Mayne*, 41 USPQ 2d 1451, 1453-54 (Fed. Cir. 1997) (emphasis added). When relying on numerous references or a modification of prior art, “it is incumbent upon the examiner to identify some suggestion to combine references or make the modification.” *id.*

The current standard for obviousness is stated below:

Our analysis begins in the text of section 103 quoted above, with the phrase "at the time the invention was made." For it is this phrase that guards against entry into the tempting but forbidden zone of hindsight, ... when analyzing the patentability of claims pursuant to that section. Measuring a claimed invention against the standard established by section 103 requires the oft difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then accepted wisdom in the field. ... Close adherence to this methodology is especially important in the case of less technologically complex inventions, where the very ease with which the invention can be understood may prompt one to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher. ... In this case, the Board fell into the hindsight trap. ... The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

In re Dembiczak, 50 USPQ 2d 1614, 1616-17 (Fed. Cir. 1999) (quotations omitted)

It is respectfully submitted that the Office action does not present any evidence for the motivation that would lead one skilled in the art to combine Murray, Beldman, Remington and Uchida ‘408.

Accordingly, for the foregoing reasons, it is respectfully submitted that none of Murray, Beldman, Remington and Uchida ‘408 disclose or suggest the subject matter of claim 3. Moreover, it is respectfully submitted that it is improper to combine any of such references because there is no motivation or suggestion for such combination to achieve the Applicants’ claimed method, and even if there were, the result would not be the method of claim 3.

Accordingly, for all of the foregoing reasons, Applicants submit that a prima facie case of obviousness over Murray, Beldman, Remington and Uchida ‘408 has not been made with respect to claim 3 because none of the three criteria of the prima facie case has been satisfied. Applicants further submit that the prima facie case also fails with respect to claims 5-8, each of

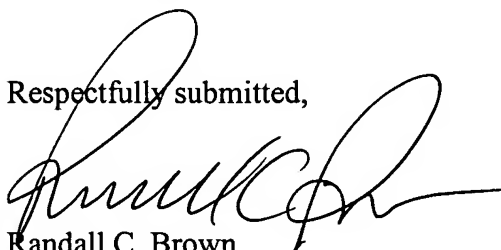
which depends directly or indirectly from claim 3 for at least the same reasons as apply to claim 3.

In view of the foregoing, Applicants request that the rejection of claims 3 and 5-8 under 35 U.S.C. §103(a) over Murray in view of Beldman, Remington and Uchida '408 be withdrawn.

G. Conclusion

It is believed that all matters set forth in the Office action have been addressed. Favorable consideration and an early indication of the allowability of claims 3 and 5-8 are respectfully requested. Should the Examiner deem that an interview with Applicant's undersigned attorney would expedite the allowance of claims 3 and 5-8, the Examiner is invited to call the undersigned attorney at the telephone number indicated below.

Respectfully submitted,



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